REMARKS

Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the amendments, remarks, and enclosures herewith. The Examiner is thanked for withdrawing the previous Office Action and for examining fusion proteins with the elected subject matter.

I. STATUS OF THE CLAIMS AND FORMAL MATTERS

Claims 1, 4-15, and 17-78 are now pending. Claims 1, 10 and 78 have been amended, and claim 79 has been cancelled herein, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

No new matter is added.

It is submitted that these claims are in full compliance with the requirements of 35 U.S.C. §112. The amendments to the claims and the remarks herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather the amendments and remarks are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Support for the amended claims can be found throughout the specification, and specifically at paragraph 36 of the specification as published (US 2004/0204352).

II. THE OBJECTION TO THE CLAIMS IS OVERCOME

Claim 1 was objected to as containing non-elected subject matter in the form of non-elected sequences. Claim 78 was objected to due to a spelling error. The objections are respectfully traversed.

The claims have been amended herein such that the objections are now moot. That is, the non-elected subject matter has been removed from claim 1 and the spelling error has been corrected in claim 78.

Therefore, reconsideration and withdrawal of the objection to the claims is respectfully requested.

III. THE INDEFINITENESS REJECTION IS OVERCOME

Claims 1, 10-15, 20 and 21 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. The rejection is respectfully traversed.

The rejection was based on part (iv) of claim 1, which recited a functional equivalent characterized by sequence homology. Although Applicants believe such language is not unclear, in the interest of furthering prosecution, the language has been removed from the claim, rendering the rejection moot.

Accordingly, reconsideration of the indefiniteness rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

IV. THE REJECTIONS UNDER 35 U.S.C. §112 ARE OVERCOME

Claims 1, 10-15, 20, 21 and 78 were rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly lacks enablement for all of the claimed elements. The rejection is respectfully traversed.

Specifically, the Office Action alleges that the specification lacks enablement for full length polypeptides or fusion proteins or fusion proteins comprising a fragment of a polypeptide of SEQ ID NOs: 16, 20, 22 or 26, that has an activity that is an antagonist to any cytokine expression and/or secretion or a functional equivalent of a polypeptide comprising the amino acid sequence of SEQ ID NOs: 16, 20, 22 or 26 that has an activity that is an antagonist to any cytokine expression and/or secretion. . However, the Office Action admits that the specification is enabled for the full length polypeptides of SEQ ID NOs: 16, 26, 20 and 22, or a fusion protein comprising a polypeptide which comprises or consists of the amino acid sequence of SEQ ID NOs: 16, 20, 22 or 26 fused to a heterologous polypeptide that has an activity that is an antagonist of TNF-alpha, IL-4, IL-6 or IL-2.

Claims 15, 20 and 21 were also rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly lacks enablement for all of the claimed elements. This rejection is also respectfully traversed. The Office Action indicates that the specification allegedly does not reasonably provide enablement for a polypeptide or fusion protein comprising a full length polypeptide for use in therapy and diagnosis of an inflammatory disease, an autoimmune disease, any generic liver disease or liver failure.

35 U.S.C. §112, first paragraph, requires that the specification describe how to make and use the invention. 35 U.S.C. §112, first paragraph, recites, in pertinent part:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same[.]

A patent claim is invalid if it is not, *inter alia*, supported by an enabling disclosure. The test for enablement requires a determination of whether any person skilled in the art can make and use the invention without undue experimentation. *See In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400, (Fed. Cir. 1988). The factors involved in determining whether there is sufficient evidence to support a finding of enablement include, among others, (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples, and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *See Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404.

Applying the law to the instant facts, all of the pending claims are enabled. As previously stated, the specification does provide guidance as to how to make and use fragments that retain the cytokine antagonist function of the full-length polypeptide and fragments of homologues that retain this function. Specifically, Applicants respectfully direct the Examiner's attention to the specification as filed at page 24, line 15 to page 25, line 3 which discloses that functionally equivalent polypeptides can be identified using the Inpharmatica Gene Threader. Further, the claims as provided herein now require that the polypeptide, at a minimum, must comprise an extracellular domain as recited in SEQ ID NO: 22. Thus, the claimed polypeptides are now described by a minimum amino acid sequence, which sequence has been found to be imperative for the activity of the polypeptide as described in the specification.

To further Applicants' argument that the pending claims are enabled, attached as Exhibit 1 is additional data furnished by the Applicants that demonstrates the necessity of the recited extracellular domain of SEQ ID NO: 22 in the claimed polypeptides.

Exhibit 1 relates to experiments carried out using the extracellular domain of INSP052, the INSP052EC protein, referred to in the present application as SEQ ID NO: 22, the cloning and expression of which is described in examples 2 and 3 of the pending application. This region is found in the INSP052 protein (SEQ ID NO: 16), and so the full length protein would share the activity identified for the active fragment upon which the experiments are based, as would other fragments containing the extracellular domain.

Example 1 from Exhibit 1 demonstrates how INSP052 modulates cytokine expression in a live mouse model. Such mouse models involving LPS-induced cytokine release are frequently used as a model for fulminant hepatitis treatment. INSP052EC is shown to decrease expression of IL-6 and TNFa. This indicates that INSP052EC could be used to treat fulminant hepatitis.

In Example 2 of Exhibit 1, INSP052EC is shown to reduce ear swelling in a model of contact hypersensitivity. This demonstrates that INSP052 is useful in treating T cell-mediated inflammation of the skin, such as found in contact dermatitis and psoriasis.

Therefore, the experimental evidence provided in Exhibit 1 shows that INSP052 is useful in treating various autoimmune/inflammatory disorders, confirming the description present in the specification regarding the usefulness of such polypetides in treating these disorders.

INSP052 is also identical to a protein described in the literature as Hepatocyte cell adhesion molecule (hepaCAM). Post-published documents such as Chung et al. (attached) and Moh et al. (attached) provide further evidence of the role of INSP052 in wound healing. Chung et al. discloses that hepaCAM increases cell spreading on the matrices fibronectin and matrigel as well as delaying cell detachment and enhancing wound healing in an in vitro wound healing assay, while Moh et al. shows that hepaCAM encodes an Ig-like transmembrane glycoprotein and is involved in cell adhesion and growth control. Both of these references further confirms Applicants description of the utility of the INSP052 protein.

Thus, when the confirmatory data attached as Exhibit 1 and the enclosed references are considered, in view of the fact that the techniques used in the present application allow highly accurate predictions of protein function to be made, the claims are clearly enabled.

To this end, the Examiner is again reminded of the text in the specification which teaches the skilled person to identify fragments that contain an immunoglobulin domain (page 8 of the application as filed) and the functional importance of this domain (page 16, line 4-9 of the application as filed). The extracellular domain of the INSP052 polypeptide contains an

immunoglobulin domain and the data presented in the examples and in Exhibit 1 attached hereto, confirm that extracellular fragments retain the activity of the full-length polypeptides. The Examiner is further reminded that fragments consisting of the extracellular domain or of exons 2 and 3 of the INSP052 polypeptide are fully enabled by the specification since they are specifically disclosed on pages 10-11, in Example 2 and in Figure 6 of the application as filed. Again, such description of the polypeptide functions in concert with the attached data and references to demonstrate enablement.

Therefore, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, are respectfully requested.

Claims 1, 10-15, 20 and 21 were rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the written description requirement. The rejection is respectfully traversed.

Initially, Applicants note that reference to "functional equivalents" has been removed from the claims as amended herein, such that any portion of the written description rejection based on "functional equivalents" is now moot.

Further, it is noted that the amended claims now require that the isolated polypeptide comprises an extracellular domain as recited in SEQ ID NO: 22. Accordingly, even in those instances where a fragment of one of the recited sequences is present, the claimed isolated polypeptide must now at a minimum comprise an extracellular domain as recited in SEQ ID NO: 22.

As described above, the specification provides ample guidance as to those species which are encompassed by the currently pending claims. Specifically, the specification does provide detailed guidance as to how to make and use fragments that at a minimum comprise an extracellular domain as recited in SEQ ID NO: 22. The recited sequence, and the conservation of that minimum sequence in each of the claimed polypeptides thus provides an adequate description of the genus of claimed compounds.

Therefore, as the Applicants have adequately defined the claimed species, and provided the teaching needs to identify members of the species, the specification provides adequate written description. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

V. THE REJECTIONS UNDER 35 U.S.C. §102 ARE OVERCOME

Claims 1, 10-15, 20 and 21 were rejected under 35 U.S.C. §§ 102(a) and 102(e) as allegedly being anticipated by Baughn et al. (WO 02/40671). Claims 1 and 78 were also rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Baughn in view of Ruben et al. (US 6,420,526). The rejections are respectfully traversed.

It is respectfully submitted that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention. *See Lewmar Marine Inc. v. Barient Inc.,* 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure of the claimed invention. *See Chester v. Miller,* 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990).

Further, it is respectfully submitted that it is well-settled that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Further still, "obvious to try" is not the standard under 35 U.S.C. §103. *In re Fine,* 5 U.S.P.Q. 2d 1596, 1599 (Fed. Cir. 1988). And, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification." Also, the Examiner is respectfully reminded that for the Section 103 rejection to be proper, **both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure**. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

As amended herein, the pending claims require that the isolated polypeptide comprises an extracellular domain as recited in SEQ ID NO: 22.

In contrast, Baughn *et al.* does not disclose the existence of an extracellular domain in the IGSFP-4 polypeptide, let alone the sequence of this domain. It does not therefore disclose a polypeptide comprising an extracellular domain as recited in SEQ ID NO: 22, and therefore fails to teach or suggest all of the elements of the pending claims.

Additionally, nothing in Ruben corrects this deficiency. Accordingly, either alone or in combination with Ruben, Baughn fails to teach or suggest all of the elements of the claims, thereby failing as a reference under both Sections 102 and 103.

Accordingly, as Baughn fails to teach or suggest all of the elements of claim 1, and as Ruben does not remedy the deficiency in Baughn, claim 1 and those claims depending therefrom, are necessarily patentable over Baughn either alone or in combination with Ruben, and the rejections must be withdrawn. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §§ 102 and 103 are respectfully requested.

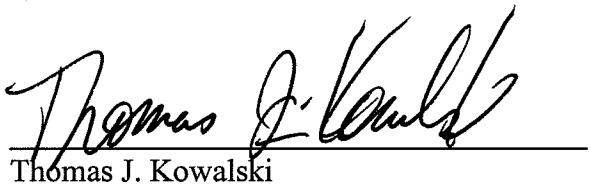
REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, prior to issuance of any paper other than a Notice of Allowance, an interview, is respectfully requested, with the Examiner and the Examiner's supervisor, and, the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the amendments, remarks and enclosures herein, the application is in condition for allowance. Reconsideration and withdrawal of the rejections of the application, and prompt issuance of a Notice of Allowance, is respectfully requested.

Respectfully submitted,
FROMMER LAWRENCE & HAUG LLP

By: 

Thomas J. Kowalski
Reg. No. 32,147
Angela M. Collison
Reg. No. 51,107
(212) 588-0800